EDISON

Oxford Biomedica

Company outlook

Vector innovation key to cell and gene evolution

Pharma & biotech

Oxford Biomedica (OXB) is a pioneer and global leader in the development and manufacture of commercial-scale lentiviral vectors (LVVs), a critical component of cell and gene therapies (CGTs). An investment in OXB gives a broad exposure to this emergent industry. During the past 12 months, OXB has effectively doubled its CDMO partner programmes to 20, while broadening its own gene therapy R&D portfolio offering. Partner Axovant expects to report six-month efficacy data on AXO-Lenti-PD (end 2020), durability of its effect in Parkinson's disease is key. Longevity to the OXB investment case rests on the growing diversity of its revenue streams and maintaining its position as an innovator. We expect OXB to lead the industrialisation of LVV manufacturing. This is critical to opening up new treatment areas where much higher vector quantities are required, especially for in vivo treatments. We value OXB at £711m.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/18	66.8	5.0	4.3	0.0	191.9	N/A
12/19	64.1	(20.9)	(16.4)	0.0	N/A	N/A
12/20e	84.2	(5.6)	(0.6)	0.0	N/A	N/A
12/21e	112.4	11.7	11.6	0.0	71.1	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Commercial vector supply driving top-line growth

The global CGT market is expanding rapidly as evidenced by further approvals and a buoyant capital market. During H120, the CGT industry attracted $10.7bn in fresh capital, a record amount despite a global pandemic. In June 2020 OXB raised gross proceeds of £40m. OXB's foresight to invest in infrastructure has doubled its production capacity, enabling a succession of deals (Juno/BMS, Beam Therapeutics, AstraZeneca) and expansion of existing partnerships (Novartis, Axovant) in the year to date. While the AZN deal is a near-term revenue contributor, the key drivers for the business are its higher margin partnerships.

Partnerships are key near-term value drivers

As a supplier of vectors for Novartis, OXB's near-term revenues are driven by both the supply of LVVs and royalties on Kymriah's escalating sales. OXB has an 18-month supply agreement with AZN for the large-scale manufacture of the COVID-19 vaccine AZD1222. OXB has received £15m upfront (capacity reservation fee) and expects to receive in excess of £35m in additional revenue. The expanded Axovant deal for AXO-Lenti-PD highlights the potential of OXB's pipeline; although high risk, this therapy has blockbuster potential for Parkinson's disease (PD).

Valuation: £711m or 892p/share

We increase our valuation of OXB to £711m or 892p/share, vs £709m previously. The major source of uplift reflects inclusion of the Beam deal and AZN COVID-19 vaccine. Under the Novartis collaboration we add a third indication for Kymriah (r/r follicular lymphoma) and a third CAR-T programme. We have pushed out the AXO-Lenti-PD launch to 2024 to reflect the status of the ongoing Phase I/II trial. We also rolled our model forward and updated FX and net cash of £50.6m (30 June).

5 October 2020

Price	**825p**
Market cap	**£678m**
	£0.78/$; £0.91/€; €0.86/$
Net cash (£m) at 30 June 2020	50.6
Shares in issue	82.1m
Free float	76%
Code	OXB
Primary exchange	LSE
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(4.1)	12.1	51.4
Rel (local)	(3.2)	17.2	79.7
52-week high/low		873p	400p

Business description

Oxford Biomedica's (OXB) LentiVector technology underpins the company's strategy. OXB generates significant revenue from partners that use its technology, notably Novartis, Juno Therapeutics (BMS), Bioverativ (Sanofi), Orchard Therapeutics, Axovant, Santen and Beam Therapeutics. OXB is also manufacturing the COVID-19 vaccine candidate AZD1222 for AstraZeneca. OXB is implementing significant capacity upgrades to enable more partnering/out-licensing agreements.

Next events

AXO-Lenti-PD six-month efficacy data	Q420
New partnership and licensing deals	2020
Spin out/out-license of in-house developed product candidate	2020

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Edison profile page

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Company description: Leader in its field

OXB is a UK biopharmaceutical company specialising in the development of gene and cell therapies; specifically, it is one of few FDA-approved LVV manufacturers worldwide. At 30 June 2020, OXB had 584 employees (expected to grow to over 650 by year end) and facilities covering approximately 226,000 sq ft. OXB currently has 20 partner programmes in its contract development and manufacturing organisation (CDMO), notably with Novartis (NOVN), Sanofi/Bioverativ, Boehringer Ingelheim and Orchard Therapeutics (ORTX). New CDMO deals announced so far this year include Juno/BMS, Beam Therapeutics and AstraZeneca (AZN) for the good manufacturing practice (GMP) manufacture of its adenovirus vector-based COVID-19 vaccine (AZD1222). CDMO partnerships provide OXB with multiple potential income streams, ranging from development and production fees, upfront milestone payments, to royalties on future product sales. In addition, OXB has five proprietary CGT assets in development. The major licensing deal with Axovant for AXO-Lenti-PD, gene therapy for PD, has effectively monetised and validated OXB's gene therapy efforts in R&D. OXB's foresight to investment in Oxbox has effectively doubled its vector production capacity, an important move given the industry bottleneck in scalable supply. We expect this combined with OXB's leading expertise in LVV development to lead to further deal announcements.

Valuation: £711m or 892p/share

We value OXB at £711m or 892p/share, vs £709m or 922p/share previously. The major source of uplift reflects the inclusion of Beam Therapeutics and the COVID-19 vaccine clinical and commercial manufacturing agreement with AZN in our valuation. We now model a third CAR-T programme under the expanded NOVN collaboration and reflect a third indication for Kymriah (relapsed/refractory (r/r) follicular lymphoma). We have updated our assumptions for other partnerships and internal assets to reflect reported changes. Our valuation is based on a risk-adjusted net present value (NPV) for partnerships with NOVN (Kymriah and two undisclosed CAR-Ts), Axovant (AXO-Lenti-PD), Sanofi/Bioverativ (haemophilia A&B), Orchard (OTL-101, OTL-201), Juno/BMS, Beam Therapeutics and AZN (COVID-19 vaccine supply) plus contributions from OXB's proprietary unpartnered product pipeline. We have rolled forward our model, updated for exchange rates and added in a terminal value of 253p/share plus net cash of £50.6m (30 June).

Sensitivities: Operational risks as growth continues

While OXB's partnership model minimises many of the usual biotech and drug development risks, it is still susceptible to clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks and financing and commercial risks. The key short-term sensitivities for OXB relate to sentiment around AZN's COVID-19 vaccine (the deal provides near-term revenue but the key drivers for the business are its higher-margin partnerships). OXB is reliant on existing partners for revenue, although diversification of income streams reduces reliance on Kymriah in the longer term. From a drug pricing and reimbursement perspective, CGTs are moving into uncharted territory and payors may prove reluctant to pay for these costly therapies.

Financials: Reinvestment and top-line growth the focus

OXB reported H120 revenues of £34m (+6% y-o-y from £32.1m) and an operating loss of £5.8m (H119 loss £6.1m). We continue to expect ongoing growth in the top line, driven in the near term by Kymriah (NOVN), and advancement of its various partnered products. OXB is in a growth phase and ongoing investment in advancing manufacturing technology and developing its pipeline are necessities to ensure future growth. We expect OXB to remain at break-even or positive operating income in the near term and as such cash of £50.6m (at 30 June 2020) should be sufficient for ongoing operations. We also expect partnering deals to be announced that will strengthen OXB's balance sheet further.

Back to the future

Since our last outlook note (In a cell and gene therapy sweet spot), we highlight the increasing pace of investment and clinical advancements made in the CGT field. CGTs are treatments of diseases by the genetic modification of a patient's cells either in vivo (gene therapy) or ex vivo (cell therapy). This represents a completely new paradigm of treatment with the potential to positively affect clinical outcomes or provide lifelong cures to intractable diseases. However, as with the advent of any transformative therapeutic class, challenges exist, whether that is efficacy vs safety trade-offs, pricing and reimbursement implications, or constraints in manufacturing.

Despite the COVID-19 background, capital markets continue to be receptive to CGT companies, with $10.7bn raised in H120 (Exhibit 1), highlighting the ongoing appetite for investment in this newly emerging sector. According to the Alliance for Regenerative Medicine, total financing in the sector was $9.8bn in 2019. M&A has been particularly strong in recent years as large and mid-cap pharmaceutical companies looked to gain or expand exposure to the CGT industry through acquisition. M&A totalled $11.3bn in 2019 ($18.9bn in 2018, $13.5bn in 2017 and $1bn in 2016), driven by Roche acquiring Spark Therapeutics for $4.3bn and Astellas acquiring Audentes Therapeutics for $3bn. This does not include BMS's $74bn acquisition of Celgene, which acquired CGT founder Juno in 2018 ($9bn). M&A activity was down in the first half of 2020, totalling $3.4bn.

Exhibit 1: Key 2020 Nasdaq IPO and secondary financings for CGT-focused biotechs

Company (ticker)	Type	Date	Amount raised ($m)	Market cap ($m)	Pipeline notes
Beam therapeutics (BEAM)	IPO	Feb	**207**	1,381.5	Pioneering the use of its proprietary base editing technology to develop a new class of precision genetic medicines and allogenic CAR-Ts. Broad and diverse portfolio targeting serious diseases. **4 preclinical assets and 7 preclinical discovery assets.**
Legend biotech (LEGN)	IPO	June	**487**	4,093.5	Developing both autologous and allogenic CAR-T and TCR-T therapies for haematological malignancies, solid tumours and autoimmune diseases. **JNJ-4528 (LCAR-B38M) BCMA-targeting CAR-T in Phase III for r/r multiple myeloma. 5 Phase I trials and 3 preclinical assets.**
Generation Bio (GBIO)	IPO	June	**230**	1,371.0	Developing a new class of non-viral gene therapies using its close-ended DNA (ceDNA) construct and cell-targeted lipid nanoparticle (ctLNP) technologies to target diseases of the liver and retina initially. **7 preclinical assets and 1 preclinical discovery asset.**
Freeline Therapeutics (FRLN)	IPO	August	**159**	546.4	Using AAV platform to develop gene therapies for chronic systemic diseases such as haemophilia and Fabry disease. **2 Phase I/II trials and 2 preclinical assets.**
bluebird bio (BLUE)	Secondary	May	**575**	3,566.1	Developing various CGTs. **Zynteglo (LentiGoblin) approved in EU for beta-thalassemia and bb2121 (ide-cel) in Phase III for 3L multiple myeloma. 1 Phase III, 3 Phase II/III, 2 Phase II, 1 Phase I/II, 5 Phase I trials and >9 preclinical assets.**
Iovance Biotherapeutics (IOVA)	Secondary	June	**604**	4,926.3	Developing autologous cellular immunotherapies using optimised tumour infiltrating lymphocytes (TIL) to target solid cancers. **6 Phase II, 1 Phase I/II and 1 Phase I trial.**
Allogene therapeutics (ALLO)	Secondary	June	**550**	5,231.8	Developing allogeneic chimeric antigen receptor T-cell (AlloCAR T) therapies using LVVs for the treatment of haematological cancers and solid tumours. **4 Phase I trials, 6 preclinical assets and multiple undisclosed preclinical discovery assets.**
Adaptimmune Therapeutics (ADAP)	Secondary	June	**259**	1,293.0	Utilising its unique SPEAR (specific peptide enhanced affinity receptor) TCR-T therapies to target a range of solid tumours. Both autologous and allogenic. **2 Phase II/III, 2 Phase I trials and 1 preclinical asset.**
Editas Medicine (EDIT)	Secondary	June	**216**	1,754.1	Developing in vivo CRISPR medicines using AAV delivery to target ocular diseases and both autologous and allogenic ex vivo CRISPR engineered cell medicines for cancers and haematological diseases. **1 Phase I/II trial, 5 preclinical assets and 4 preclinical discovery assets.**

Source: Company websites, EvaluatePharma. Note: AAV: adeno-associated virus. Market capitalisation at market close on 1 October 2020. Assets in preclinical discovery are pre-lead optimisation.

As of September 2020, seven CGT products had received FDA/EMA approval in oncology, ophthalmology and rare hereditary disease indications. The first wave of CGT products to commercially launch in 2017 were ex-vivo CAR-Ts Kymriah (NOVN) and Yescarta (Gilead/Kite pharma), and in vivo gene therapies Strimvelis (Orchard Therapeutics) and Luxturna (Spark Therapeutics). 2019 approvals include bluebird bio's gene therapy Zynteglo (LentiGoblin), which received EMA approval for transfusion dependent beta-thalassemia, and AveXia/NOVN's gene therapy Zolgensma for paediatric spinal muscular atrophy. So far in 2020, the FDA has approved a

third CD19-targeting CAR-T, Kite/Gilead's Tecartus, for relapsed or refractory mantel cell lymphoma (MCL).

Sparking the pricing and reimbursement debate

As additional CGT therapies have made it to market, there remains ongoing focus on pricing and reimbursement. It is widely recognised by payors and prescribers that gene therapies could provide huge clinical benefit and in some conditions be curative, but the high potential cost of such therapies remains of concern. Zolgensma's pricing at $2.1m, 2019 sales $361m (the most costly single dose drug in history), has focused patients, prescribers and payers on price, reimbursement and the value of the outcomes generated by these potential 'once-and-done' therapies.

In the US, the fragmented healthcare system has generated varied and distinct reimbursement challenges for Kymriah. Reimbursement discussions with the Centres for Medicare and Medicaid Services (CMS) are ongoing and the CMS has recently announced a Medicare severity diagnosis related group (MS DRG) for CAR-T therapies. The CMS has to date only committed to partial coverage of the total cost (including hospitalisation costs) of treatment with CAR-T therapies. The hospital reimbursement list price of a CAR-T therapy is ~ $373,000, but once additional costs are factored in the actual cost is $50,000 higher and this significant cost has to be absorbed by hospitals and the patients.

Payors and insurers are addressing the cost impact of gene therapies, for example in the CVS Health white paper Gene therapy, Keeping costs from negating its unprecedented potential, and concluding that gene therapies could provide huge clinical benefit and in some conditions be curative, but the high potential cost of such therapies needs to be addressed ahead of the anticipated launches in 2021 of treatments for more common genetic disorders (such as haemophilia A and B). Not only is the cumulative cost of treating higher patient numbers a concern, but other challenges faced by payors are the unknown factors including durability of treatment. In addressing the latter, value-based contracting remains appealing; this is when the manufacturer agrees to refund a portion of the costs of the treatment if the patient fails to achieve and sustain an expected clinical response; this directly links reimbursement to outcome. The duration of the response to the therapy or the length of the cure to the patient would lead to incremental payments, perhaps annually, based on its continued success. In central-payer markets such as the UK, where patients can be closely followed, this is not likely to be difficult, but in much larger fragmented markets such as the US, where patients can move jobs (and therefore health insurers) across the country, monitoring the duration of their responses and therefore the reimbursement to the drug manufacturer could be problematic. Bluebird bio has proposed an instalment payment plan for its Zynteglo (LentiGoblin) gene therapy; insurers can pay the cost of therapy over up to five years. Bluebird bio will charge an initial upfront payment but will only be entitled to receive the rest of the cost if the patient continues to see benefit. Despite issues about access, uptake of CGTs has been strong during H120 (Kymriah sales of $211m and Yescarta sales of $296m). However, we note that approved CGTs target modest patient populations and issues will surmount as approval rates ramp up particularly in more prevalent conditions. To that end, the industry must address the industrial production costs of CGTs, akin to the industrialisation of monoclonal antibodies during the last few decades.

Industrialisation of vector production is key to lowering cost of goods

CGT manufacturers are looking to the future: critically how manufacturing processes can be streamlined and industrialised to drive down costs of goods (in the development and fulfilment of scalable, affordable manufacture of LVVs). Biopharm Services estimates that the cost of manufacturing a CAR-T cell therapy for a single patient to be ~ $100,000–150,000, of which the viral vector components cost about 30% (although this is product specific). This compares to 5–20% cost of goods sold for small molecule drugs or antibody-based treatments. We believe these

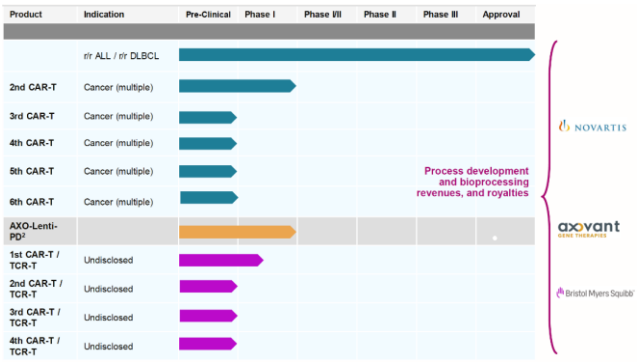
original high vector costs reflect the initial costs of manufacturing a CAR-T (under Process A) and these costs have been brought down significantly by moving from Process A to higher-yield Process B manufacturing. The manufacture of CGTs is complex, with companies facing many challenges, particularly for autologous therapies with complicated supply chains, and manufacturing processes create a bottleneck in the ability to scale. In terms of viral vectors (a critical component of CGTs), current demand is outstripping global scalable supply particularly in the field of LVVs.

As the industry bottleneck in scalable manufacturing technologies and processes remains more relevant than ever, the innovators in the field with established fully integrated manufacturing processes (from preclinical to commercial supply) are set to benefit. OXB remains one of few companies that fulfil this criterion. OXB continues to innovate within its platform capabilities and its proprietary gene therapy R&D pipeline as it drives the industrialisation of vectors towards better yields and lower cost of production. OXB's successful transition to Process B bioreactor vector production for Kymriah (a tenfold yield and tenfold efficiency increase over Process A) in H119 demonstrated its expertise in vector manufacturing. Moving to Process B bioreactor vector production also enabled deals such as Bioverativ (Sanofi), given the large number of vectors needed for the treatment of conditions such as haemophilia (liver). In March 2019 OXB announced a collaboration with Microsoft Research to utilise its machine learning technology to develop insights into OXB's processes; the aim is to improve the yield and quality of OXB's next-generation gene therapy vectors.

New collaborations add to the CDMO revenue mix

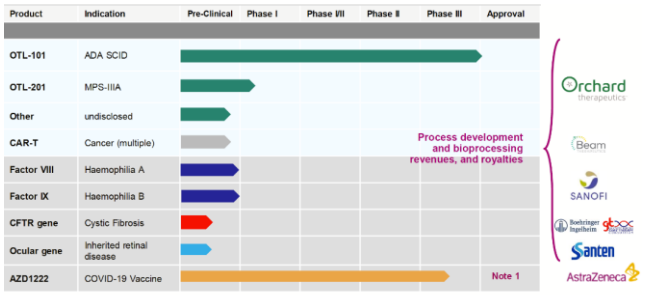
The continued signing of development, manufacturing and licence agreements provides OXB with a diverse and broad income stream from its platform technology. OXB has more than doubled its number of CDMO partnered programmes to 20 in the last 12 months. In December NOVN extended its commercial supply agreement by five years and OXB now provides six LVVs to support NOVN's CAR-T portfolio. This provides strong endorsement of OXB's industry leading capabilities given that NOVN has recently invested in its own CGT cell processing capabilities (for the vein-to-vein process for its CAR-T franchise). The major five-year clinical supply agreement with Juno (BMS) is the second major CGT partner signed by OXB and covers four undisclosed CAR-T and TCR-T programmes. Juno is one of the pioneers in the CGT industry. OXB has additionally signed clinical and commercial supply agreements with Beam Therapeutics and AZN. Exhibits 2 and 3 highlight the current pipeline of partnerships. Multiple deals reduce the concentration of risk and offer an investor exposure to a diverse range of CGT products at varying stages of development. In addition to CDMO activities, OXB is targeting the spin out/out-license of one in-house product candidate from its proprietary pipeline, which has been validated through the out-licensing of AXO-Lenti-PD to Axovant in 2018.

Exhibit 2: OXB's CDMO pipeline



Source: OXB corporate presentation. Note: 1) USAN name is tisagenlecleucel. 2) AXO-Lenti-PD formerly known as OXB-102, which OXB out-licensed to Axovant.

Exhibit 3: OXB's CDMO pipeline



Source: OXB corporate presentation. Note: 1) Potential scale up and vaccine manufacturing revenues.

Novartis's Kymriah the start of more CAR-Ts to come

OXB is now working on six different LVVs for use in NOVN's CAR-T products. OXB's partnership with NOVN began in 2013, when NOVN signed a manufacturing agreement to produce clinical trial material for its CTL019 clinical development programme. The first deal was specifically to manufacture batches of clinical material and demonstrate process development and manufacturing services capabilities bespoke to the cell (or gene) therapy. CTL019 or Kymriah, a CD19 targeting CAR-T, was the first cell therapy to be approved in the US in August 2017 for paediatric B-cell precursor acute lymphoblastic leukaemia (pALL) (it is now approved in over 25 countries worldwide including the US, EU, Australia, Canada and Japan for adult patients with DLBCL as well as pALL).

In October 2014, NOVN signed a process and manufacturing deal (for CTL019) worth $90m over three years ($14m upfront including a $4.3m equity subscription, $76m in milestones over three years and undisclosed royalties); this was a major validation of OXB's LentiVector platform technology capabilities. In June 2017 as CTL019 (Kymriah) moved towards commercialisation, NOVN signed a new commercial supply agreement for CTL019, which included $10m upfront and in excess of $90m in additional revenue over the next three years. NOVN is currently dependent on OXB for its vector supply, which is a critical part of the Kymriah manufacturing process and, as its technology and manufacturing process was involved in the regulatory application and subsequent approval of Kymriah, we believe it is extremely unlikely that NOVN will switch supplier.

Five-year expansion and six CAR-T programmes in place

In December 2019 the collaboration with NOVN was extended, with NOVN committed to paying OXB a minimum of $75m (for vector batches) in manufacturing revenue over the five-year extension. OXB will also receive commercial development fees on the five programmes in development. Additionally, it will be paid a mid-single digit £m facility reservation fee and has agreed to dedicate part of its 84,000 sq ft Oxbox manufacturing facility to NOVN, while also ensuring that at least two of its GMP facilities are capable of commercial supply, essentially ensuring a dual-sourced supply if the need arose. The extended deal means OXB is now working on six different LVVs for use in NOVN's CAR-T products. While the targets are undisclosed by OXB, we assume (based on NOVN's November 2019 R&D day) that targets include CD19, BCMA, CD22, IL3RA (also known as CD123) and EGFRvIII. During Q120 NOVN added the sixth programme to the mix, and we now include a third CAR-T in our forecasts, in addition to existing forecasts for Kymriah (across multiple indications) and a second CAR-T (which we assume is for multiple myeloma).

Follicular lymphoma the next potential indication for Kymriah

NOVN reported Kymriah sales of $211m H120 (vs $103m in H119) across approved indications of pALL and DLBCL. NOVN reported there was no interruption of supply during COVID-19. NOVN continues its global rollout of Kymriah and we note that 250 qualified treatment centres and 25 countries worldwide have coverage for Kymriah for at least one indication. In August NOVN released positive data from the interim analysis of the pivotal Phase II ELARA trial evaluating Kymriah in r/r follicular lymphoma; the study met its primary endpoint (complete response rate), and no new Kymriah safety signals were observed. ELARA will form the basis of US and EU regulatory submissions (expected 2021). We note Kymriah was granted regenerative medicine advanced therapy (RMAT) designation in the US for this indication and we forecast approval in 2022.

Follicular lymphoma is the second most common form of non-Hodgkin lymphoma (NHL), and represents ~22% of NHL cases. While the advent of novel treatments has improved overall survival, many patients relapse or remit, such that patients may receive up to a median of five lines of prior treatment. Kymriah could have utility in these patients who are refractory to treatment or relapse on existing treatment options.

Novartis valuation assumptions

For the NOVN partnership our model included opportunities for Kymriah in pALL and DLBCL. We add in the r/r follicular lymphoma indication for the first time. Our prior model assumptions included an undisclosed CAR-T asset, which we have assumed is MCM998, a BCMA-targeting CAR-T for use in patients with multiple myeloma (NOVN is developing a BCMA and CD19 CAR-T combination). Following the expansion to the NOVN collaboration, we have added a third CAR-T programme (undisclosed but we assume CD22 for adult ALL). We forecast that OXB will sell vector batches to NOVN for $1.5m per batch, with peak gross margins of 30%. We highlight that further collaboration on CAR-T assets between OXB and NOVN is possible as NOVN continues to invest heavily in its CGT capabilities. We assume a $7m (c £5.2m) reservation fee will be spread across the five-year contract with no financial impact until 2021 under the expanded collaboration agreement.

Juno deal strike two for Oxbox investment

US-based Juno Therapeutics (part of BMS Group) is one of the main pioneers in CAR-T development. Juno has been developing a broad pipeline of CAR-T and T-cell receptor T-cell (TCR-T) programmes in oncology and other indications spanning preclinical, clinical trials and a biologics licence application (BLA) filing for its most advanced asset, liso-cel (JCAR017).

Multiple value streams to the Juno deal could grow further

Under the terms of the Juno deal, OXB received an upfront payment of $10m in cash. OXB is eligible for up to $86m upon achievement of certain development and regulatory milestones spread across four undisclosed assets (we assume that these are focused on CAR-T or TCR-T assets in preclinical and clinical development and may include one of the CD22, WT1, L1CAM and MUC16 programmes) over multiple potential indications (discussed below). In addition, OXB is eligible to receive up to $131m in sales-related milestones plus an undisclosed royalty on the net sales of products sold by Juno utilising OXB's LentiVector platform. OXB is working on four assets covering multiple indications; this is a non-exclusive deal, thus OXB can supply LVVs for these targets to others. In addition to milestones, OXB will be paid for its bioprocessing and commercial development work.

We expect multiple revenue streams from the partnership to include bioprocessing (the sale of vector batches) revenues and development milestones in addition to payments from process development and scale-up projects. If Juno's pipeline progresses towards regulatory approvals and launch, then we would expect this mix to alter as the royalty stream builds. This is an initial deal with Juno and as these assets progress towards commercial viability, we would expect additional deals to cover commercial manufacturing supply. However, our caveat remains that much of Juno's pipeline is at the proof-of-concept stage. For the Juno partnership we have modelled the opportunity for JCAR018 only, for illustrative purposes, given the assets are undisclosed; we will revisit our assumptions as we gain more visibility as time progresses.

Beam Therapeutics' next-generation gene therapy

US biotech Beam Therapeutics is focused on developing precision genetic medicines utilising its proprietary base editing technology, a highly innovative next-generation CGT technology. The pipeline is very early stage (preclinical) and focused on a range of therapeutic areas: hemoglobinopathies, oncology, liver disease, ophthalmology and CNS. In August Beam signed a development, manufacture and license agreement (DMLA) granting it a non-exclusive licence to OXB's LentiVector platform for application in next-generation CAR-T programmes in oncology. A

three-year clinical supply agreement (CSA) is also in place for OXB to provide clinical trial material to Beam, in return for LVV development and clinical trial manufacturing supply payments. OXB will receive an undisclosed upfront payment (we assume $5m in cash) and is eligible for undisclosed development and regulatory milestones initially covering one asset, but with potential to extend to more. In addition, OXB is eligible to receive an undisclosed royalty on the net sales of products sold by Beam that utilise OXB's LentiVector platform. OXB is currently undertaking work on one preclinical asset with Beam; we note the agreement allows for the parties to initiate additional projects in the future.

Given the preclinical nature of Beam's assets and its novel technologies (base editing and allogenic CAR-T), the time to market is longer than more recent deals such as that with Juno. However, we believe that this collaboration will enable OXB to work towards next-generation products. Beam's base editing technology has the potential to enable a new class of genetic medicines where a specific single base in the genome is corrected (point mutations or genetic error of a single base make up ~58% of all known errors associated with disease). Beam's approach targets a single base in a genome without making a double-stranded break in the DNA, unlike established gene editing technologies (eg CRISPR). Beam is currently developing a diversified portfolio of 12 base editing programmes against distinct targets and is evaluating optimal clinically validated delivery approaches for each programme. While OXB has not disclosed the exact details of the project it is working on, we believe the relevant product appears to be the engineered allogeneic (or off-the-shelf) CAR-T products, via multiplex editing of T-cells from healthy donors. These ex vivo gene therapies benefit from the use of LVV to deliver a target gene (presumably for the CAR) as they integrate into the host cell genome (as appose to AAV) so the target gene is maintained when the cells are expanded (cultured to divide and multiply), prior to administration. In vivo gene therapies however, could utilise either LVV or AAV vectors.

AZN COVID-19 vaccine opportunity for Oxbox

In May OXB signed an initial one-year clinical and commercial supply agreement with AZN for AZD1222 (previously called ChAdOx1 nCoV-19), a potential vaccine against COVID-19 developed by a consortium led by the Jenner Institute, Oxford University. Under the agreement, OXB will provide multiple batches of the prospective vaccine, the majority of which are expected to be produced before the end of 2020. OXB has already commenced production in one of its newly equipped GMP suites at Oxbox. AZD1222 relies on adenoviral vector technology, but OXB has leveraged its LVV expertise to provide adenoviral vectors. This highlights the company's vast experience in vector manufacturing, as well as its flexibility and capabilities beyond the LVV space in which it is a global leader. AZN has additional deals with other manufacturers, including Catalent and Emergent BioSolutions, to meet the large-scale manufacturing needs and potential global demand upon successful completion of clinical trials.

AZD1222 a front runner in the global COVID-19 vaccine race

The AZN agreement with the University of Oxford covers the global development and distribution of AZD1222. The vaccine is currently in late-stage global clinical trials (including UK and US sites) and AZN has indicated that it is aiming for a 50% efficacy rate, which is in line with the threshold set by the FDA and similar to that achieved by the UK flu jab over the last couple of years. We note that the clinical trials were put on hold at the start of September due to a suspected case of transverse myelitis, a syndrome characterised by inflammation of the spinal cord and neurological dysfunction, in one participant in the UK trial. This is a routine occurrence in the case of an unexplained illness and the UK trial resumed less than a week later. However, the US trial is still on hold while the National Institutes of Health completes its investigation. AZN expects the first cut of pivotal data to

be available for submission before year end, making it a frontrunner in the race to bring a COVID-19 vaccine to market.

AZD1222 uses a replication-deficient and weakened version of a common cold adenovirus (ChAdOx1) that causes infections in chimpanzees. The recombinant adenovirus vector has been modified to contain the genetic material for the SARS-CoV-2 (the virus that causes COVID-19) spike glycoprotein, which has been shown to bind to ACE2 receptors on human cells to gain entry, a key step in the virus's pathogenesis. Following vaccination, the surface spike glycoprotein is produced, triggering an immune response and priming the immune system to recognise and attack any future infection, in theory conferring immunity against COVID-19.

AZN published Phase I/II (n=1,077) clinical data in July that confirmed that AZD1222 elicited a neutralising antibody response at a level similar to convalescent COVID-19 patients after a single dose in 91% of patients (after one month) and 100% after a second dose. The spike-specific T-cell responses peaked on day 14 and were maintained up to day 56. These read outs are equally important as it is currently not known whether antibody responses or T-cell responses are indicative of protective immunity. No serious adverse events were reported, and all side effects were deemed mild to moderate. However, despite potential advantages over other vaccine technologies, adenovirus vector vaccines (AZD1222) can trigger an immune response that can hinder efficacy, due to pre-existing immunity to common adenovirus infections such as tonsillitis, gastroenteritis and conjunctivitis.

Other Phase III stage COVID-19 vaccine developers include Moderna and Pfizer/BioNTech. These companies are developing mRNA-based vaccines and we note that to date no commercial products utilising the same mRNA technology have been approved for use.

AZN deal to boost revenues in FY20 by more than £10m

In September OXB announced an 18-month supply agreement with AZN for the large-scale manufacture of the vaccine. This is under a three-year master supply and development agreement, which has the option to extend the supply period for a further 18 months into 2022/23. OXB has received £15m upfront from AZN as a capacity reservation fee. OXB expects to receive more than £35m additional revenue contingent on continuation of the vaccine programme and satisfactory scale-up of manufacturing capacity, plus specific material costs for the manufacture of AZD1222 until the end of 2021. In total OXB expects the AZN deal to boost revenues in FY20 by more than £10m, subject to successful scale up of manufacturing.

OXB will reserve up to three manufacturing suites at Oxbox, its 84,000 sq ft bioprocessing facility, capable of manufacturing up to 1,000L scale. As a result of the collaboration with the UK's Vaccine Manufacturing Innovation Centre (VMIC), OXB plans to bring two new manufacturing suites online significantly earlier than was originally planned. This has only been possible because of previous investment in its Oxbox facility. OXB expects all four manufacturing suites in the first phase of Oxbox development to be in operation by early Q420. The deal with AZN only provides potential upside for OXB as it has no capital at risk (reimbursed by AZN through government grants) and will benefit from the £15m upfront reservation fee plus any revenues from any development work, although OXB is charging a reduced rate compared to normal.

OXB gains exposure to adenoviral vector manufacturing

OXB is gaining exposure to manufacturing adenoviral vectors on 1,000L scale, which is significantly larger than the current LVV manufacturing scale (200L). OXB is using the downstream process outlined by the consortium, which uses similar purification techniques (such as hollow fibre and anion exchange purification) to LVV manufacturing. This valuable knowledge exchange will stand OXB in good stead if it was to pursue the manufacturing of adenoviral vectors in the future. Additionally, OXB is acquiring knowledge of scaling up from 200L to 1,000L, which it can apply to

LVV manufacturing. We note OXB's current preference for LVV manufacturing as it is able to incorporate its IP into manufacturing contracts, which leads to higher royalty rates.

Other partnership updates

Orchard Therapeutics' refocused strategy

ORTX (a UK/US-based biotech) focuses on the treatment of rare diseases. It has two products in development under its manufacturing agreement with OXB: OTL-101 for adenosine deaminase severe combined immunodeficiency (ADA-SCID) and OTL-201 for Sanfilippo A syndrome. Despite overwhelming positive data in ADA-SCID, published in 2019, the newly appointed CEO at ORTX (Bobby Gaspar) has reprioritised ORTX's portfolio to focus on neurometabolic disorders. Additionally, ORTX is investing in next-generation manufacturing through its licence agreement with GSK for proprietary lentiviral stable cell line technology (as these programmes were out-licensed by ORTX from GSK) and has extended its manufacturing partnership with MolMed (manufacturer under GSK) through to June 2025. As such OTL-101 has been deprioritised (we have therefore pushed out launch to 2024 from 2022). We note OTL-101 has received both breakthrough therapy designation and rare paediatric disease designation from the FDA. Orchard continues to develop OTL-201 (ex vivo autologous gene therapy being developed for the treatment of MPS-IIIA, Sanfilippo A syndrome); the proof of concept study is enrolling, and interim data are expected in 2021.

Sanofi returns ocular gene therapy assets; Bioverativ tie up ongoing

OXB's historical partnership with Sanofi for out-licenced ophthalmology assets SAR422459 (Phase I/II for Stargardt) and SAR421869 (Phase I/II for Usher) has been terminated. Sanofi has informed OXB it intends to returns the rights to both ocular assets to OXB. This follows the decision in 2019 to halt the ongoing clinical development for SAR421869 following a strategic portfolio review. We have removed both assets from our forecasts and will readdress this when new guidance becomes available (OXB will undertake an internal review once the assets are returned).

OXB's partnership with Sanofi through its deal with Bioverativ is ongoing and unaffected. In March 2018, OXB signed a partnership deal with Bioverativ (acquired by Sanofi for $11.6bn in early 2018) to develop in vivo gene therapies for haemophilia A (Factor VIII deficiency) and haemophilia B (Factor IX deficiency). OXB received $5m on the closure of the deal and is entitled to up to $100m in revenue from product development, regulatory and sales milestones, in addition to undisclosed royalties. Bioverativ's gene therapies are in preclinical trials, and Sanofi has recently communicated it expects both assets to move into the clinic in 2022. Our model assumes these gene therapies could launch in 2026 (from 2025), with accelerated approval after completing Phase II trials. We believe the focus on LVV may prove an advantage as durability of effect of gene therapies in haemophilia has been in the spotlight, given cost per treatment.

We note that in August 2020 competitor BioMarin received a complete response letter from the FDA for its AAV gene therapy valoctocogene roxaparvovec (BMN 270) for haemophilia A. Notably BioMarin states the FDA have introduced a new recommendation for two years follow-up data from the ongoing Phase III (BMN 270-301) study to provide substantial evidence of a durable effect using annualised bleeding rate as the primary endpoint. BioMarin presented four-year follow-up data from the ongoing Phase I/II study at the World Federation of Hemophilia virtual summit in June. All patients had severe haemophilia prior to treatment (defined as Factor VIII activity ≤ 1IU/dL). Although 86% of patients in the high dose cohort (n=7 at 6e13vg/kg dose) were bleed-free at four years, the mean Factor VIII activity level consistently decreased year-on-year (year 1: 64.3IU/dL, year 2: 36.4 IU/dL, year 3: 32.7IU/dL, year 4: 24.2IU/dL) as measured by the CS assay. This clearly raises durability questions around whether the Factor VIII activity may drop to a point

where it no longer provides protection from bleeds, a serious concern for a treatment that could cost $2–3m.

Product candidates being developed by Bioverativ and OXB could gain significant market share if they are able to improve on the AAV products in development. Although cell turnover in the liver is slow, LVVs may have a potential advantage as they integrate into the host cell genome and the target gene is therefore maintained as cells divide, potentially increasing durability.

Haemophilia A and B are indications with significant patient populations. Haemophilia A is approximately four times as common as B and is estimated to occur in approximately one in every 5,000 male births. Worldwide incidence is currently estimated to be approximately 400,000 cases. The gene therapies that OXB and Bioverativ are developing would encode for either Factor VIII (if addressing haemophilia A) or Factor IX (if addressing haemophilia B). LVVs that carry the appropriate genes would be injected into a patient either systemically or directly into the liver. These vectors would then insert the specific gene into the appropriate cells in the liver, such that they are able to produce Factor VIII or IX proteins. To address the liver would require huge quantities of vector; as such, we expect that in order to meet both the large patient numbers and large individual doses, OXB would need to use bioreactors in combination with its other proprietary technologies such as its Transgene Repression in Vector Production (TRiP) system, SecNuc technology and LentiStable cell lines that provide improved vector yields and scalable, cost-effective manufacturing. Due to the requirement to utilise OXB's proprietary technologies to deliver gene therapies on this scale, we forecast that OXB is likely to receive a higher royalty rate than it receives from products that require smaller vector quantities, eg Kymriah in pALL or DLBCL.

Currently, patients with haemophilia are treated directly with the missing clotting factors by regular injections. This is a multi-billion-dollar market, with global sales from both haemophilia A and B drugs totalling approximately $11.1bn in 2019 (source: EvaluatePharma).

Gene therapeutics portfolio coming of age

OXB has completed a review of its internal pipeline and now has five internally generated assets that are in preclinical development (Exhibit 4) and one out-licensed product in Phase I/II. OXB-302 (CAR-T 5T4) remains the priority candidate in preparation to enter clinical-stage testing in the next 12 to 18 months and work on OXB-201 (wet age-related macular degeneration (AMD)) and OXB-202 (corneal graft rejection) has been discontinued. OXB-203 takes over from its predecessor OXB-201 for wet AMD, preclinical work on OXB-204 (Leber's congenital amaurosis variant 10 (LCA10)) and OXB-103 (amyotrophic lateral sclerosis (ALS)) is continuing, and a new preclinical programme, OXB-401 (liver indication), has been initiated. Management is targeting the spin-out/out-license of one in-house product candidate during 2020. We note that gene therapies that target neurological or ophthalmological indications remain highly attractive, often due to the significant unmet need. The out-licence agreement achieved with Axovant for AXO-Lenti-PD (previously known as OXB-101) demonstrates the scale of economic terms reached previously, although we note the unmet need and large patient population in PD as the driver for the large deal terms.

Exhibit 4: OXB's proprietary pipeline

Product	Indication (area)	Stage of development	Notes
OXB-302	Multiple haematological and solid tumours (oncology)	Preclinical	Leverages OXB's LentiVector technology to generate a 5T4 targeting CAR-T therapy, which has scope to treat a plethora of cancers. 5T4 is a heavily glycosylated cell surface protein expressed on various haematological tumours as well as most solid tumours, but has low levels of expression on non-cancerous tissues, making it an attractive therapeutic target. OXB has also demonstrated 5T4 is expressed on cancer stem cells, which are responsible for metastasis and relapse. 5T4 targeting therapies as a class have demonstrated some exceptional efficacy, counterbalanced by a high incidence of severe side effects. Preclinical studies are nearing completion and OXB-302 has demonstrated in vitro activity in haematological tumour cell lines and both in vitro and in vivo (mouse) efficacy in various ovarian cancer models.
OXB-203	Wet AMD (ophthalmology)	Preclinical	Uses OXB's LentiVector technology to deliver a gene that encodes for aflibercept (a VEGF-trap) into the eye. OXB-203 has the potential to be given as a single 'one-and-done' treatment, significantly reducing the injection burden for wet AMD patients. This asset builds on the ongoing long-term follow-up Phase I study of its predecessor OXB-201, which has demonstrated stable expression of both endostatin and angiostatin out to six years so far, underlining the duration of response OXB's LentiVector technology can provide. OXB-201 development was halted in favour of OXB-203 and the VEGF-trap approach, which is seen as a better validated target for wet AMD. Preclinical proof of concept data in rat models are encouraging and long-term PK studies are still ongoing.
OXB-204	LCA10 (ophthalmology)	Preclinical	Lentiviral-based gene therapy for the rare inherited eye disease LCA10 (Leber's congenital amaurosis variant 10), which causes light sensitivity, nystagmus and a reduction in peripheral vision. LCA10 is caused by defects in the CEP290 gene, which we assume OXB-204 is targeting, and there are currently no approved treatments for this disease. We note that competition include ProQR Therapeutics' sepofarsen, currently in Phase II/III, and Allergan/Editas Medicine's EDIT-101, currently in Phase I/II.
OXB-103	ALS (neurology)	Preclinical	Lentiviral-based gene therapy for ALS, a rare progressive neurological disorder that affects motor neurons, resulting in cell death. ALS has multiple causes but the most common contributory genetic defects are C9orf72 and SOD1. We expect OXB-103 will look to correct one of these genetic defects. Treatment options are currently limited to four FDA-approved drugs that may slow disease progression but there are currently no approved curative therapies. We note BrainStorm Cell Therapeutics' stem cell therapy NurOwn is currently in Phase III.
OXB-401	Undisclosed liver indication	Preclinical	Early stage preclinical development of OXB-401 was recently initiated. The genetic target and type of liver disease has not been disclosed yet. We assume OXB-401 is a gene therapy that uses OXB's LentiVector technology to correct a genetic defect that drives the pathology of the chosen liver disease.

Source: Oxford Biomedica, Edison Investment Research.

Axovant: Aiming for a breakthrough in PD

In June 2018 OXB signed an out-licensing deal with Axovant for its PD gene therapy AXO-Lenti-PD (previously OXB-102) in a deal worth up to $842.5m in development and sales milestones ($30m upfront payment, $55m in development milestones and over $757.5m in regulatory and sales milestones) plus 7–10% tiered royalties on sales. In July 2020 this partnership was extended with a three-year CSA for the manufacture and supply of AXO-Lenti-PD.

AXO-Lenti-PD is a re-engineered version of OXB's gene therapy ProSavin (OXB-101), which has previously completed a Phase I/II open-label study in 15 patients and demonstrated statistically significant improvements in motor behaviour. In January 2020 Axovant reported 12-month data from cohort one of the Phase I/II SUNRISE-PD study, which demonstrated a 37% improvement in motor function from baseline as assessed by the UPDRS Part III 'OFF' score (this followed an improvement of 29% at six months on the same scale). Axovant expects to present six-month efficacy data from the six patients dosed in cohort one and two in its SUNRISE-PD clinical study by Q420, and commencement of the sham-controlled portion of the study is expected in 2021.

We believe Axovant will aim to launch the therapy based on the Phase II data from the ongoing SUNRISE-PD study plus historical ProSavin data with an accelerated approval. Feedback from a pre-IND meeting with the US FDA in December 2018 indicated the data from the ProSavin trials might be supportive of the planned BLA regulatory path. Previously, Axovant had communicated potential launch in 2022. However, this has not been confirmed in recent presentations, and we have therefore moved our forecast launch date back by two years to 2024 to better reflect the status of the ongoing Phase I/II trial.

OXB's leading viral vector positioning

Cell and gene therapies use vectors to deliver genetic information into a patient's cells; the two types of vector most commonly used are LVV and AAV. Viral vectors can infect human cells; once LVVs are inside the cytoplasm of a cell they utilise their own reverse transcriptase to make DNA from their single-stranded RNA genome. This DNA is then integrated into the genome of the host. AAVs can also infect human cells and express their chosen transgene, but the DNA is not integrated into the host cell's genome, which can lead to a reduced duration of expression and response to AAV-based therapies. The body also has an innate immune response to AAVs that potentially limits the efficacy of the technology. LVVs can carry approximately twice the genetic payload compared to AAV, allowing the transfer of larger or multiple genes (up to 10kb).

Not all viral vector systems are equal

Unlike some viral systems, lentiviruses have an ability to infect both mitotic (dividing) and post-mitotic (non-dividing) cells. Post-mitotic cells are unable to be infected by most retroviruses, which give lentiviruses a unique advantage; however, competing technologies do exist such as adeno-associated viruses, which are able to infect non-dividing cells. Post-mitotic cells include neuron and muscle cells that can be found in the brain, heart and skeletal muscle. These cells are key targets for neurological and cardiac diseases.

LVV and viral vectors in general are modified viruses that efficiently infect a target cell but are rendered replication deficient. Replication deficient viral vectors are a must; as such, regulatory requirements covering lentiviral technology are strict, ensuring that generic contract manufacturing organisations and biotech companies entering the field have a high technical barrier to entry. Under FDA rules, for LVV products to be utilised in humans, there must be an absence of replication-competent lentivirus. LVVs have evolved through multiple generations as they have been modified to become safer and more efficient. The generations are defined by what genes of the lentivirus are retained and how they are packaged. The most recent third-generation vectors removed all accessory genes that aided in virulence and pathogenicity while splitting the remaining genes, which are vital for expression of the transgene across three plasmids.

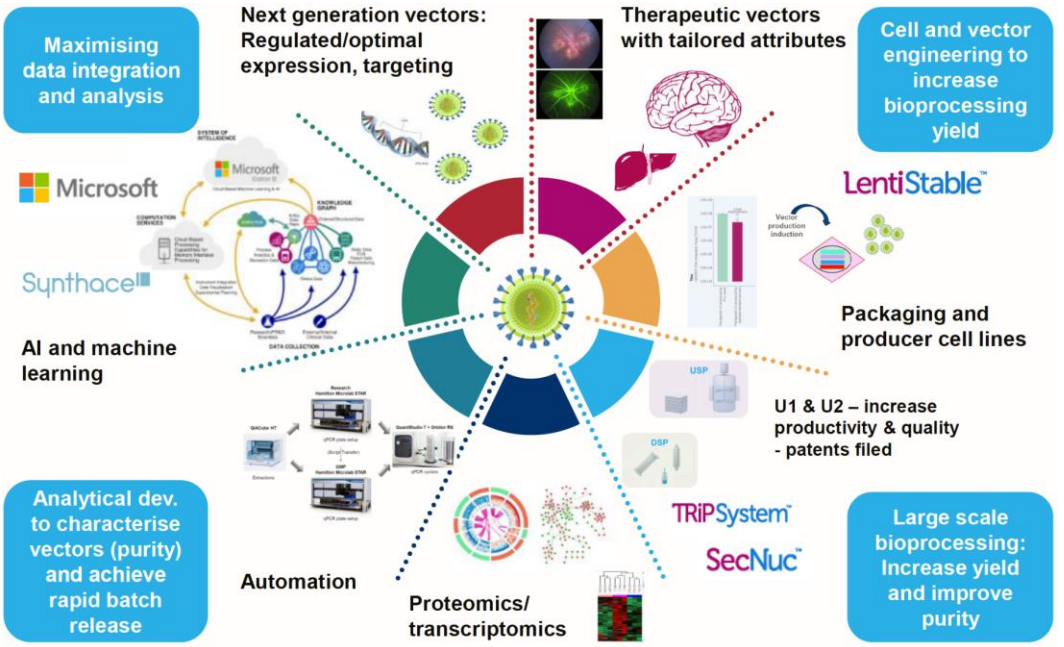
Early innovation enables future growth

OXB is leading the industrialisation of lentivector manufacturing through significant capacity expansions and continued process innovation. Increasing manufacturing efficiency is key as CGTs move from treating rare diseases of small organs such as the eye, which requires smaller quantities of vector, to more common diseases of larger organs like the liver and lungs, which require much larger quantities of vector.

In 2019 OXB successfully transitioned manufacturing from adherent cell lines (Process A) to Process B serum-free suspension bioreactors (200L), furnishing a 10-fold increase in yield. Bioreactors bring multiple benefits including dramatically increased capacity, as well as reduced labour and cost of goods. Bioreactors offer the ability to better control the manufacturing conditions and the transition to a serum-free chemical media removes the effects of serum batch variability, which increases the consistency of the process.

To move further along the efficiency pathways, the group has continued to focus on developing, refining and enhancing its technology through advances such as its next-generation TRiP manufacturing system, SecNuc technology and LentiStable cell lines that provide improved vector yields and scalable, cost-effective manufacturing (Exhibit 5).

Exhibit 5: OXB's innovation wheel



Source: OXB corporate presentation

Cell and vector engineering to increase bioprocessing yield

LentiStable cell lines are a result of more than 15 years of optimisation work and offer a simplified, cost-effective and scalable manufacturing process in comparison to a transient transfection process. LentiStable producer cell lines integrate all components (target, packaging and envelope transgenes) into the cell genome and enable multiple harvests of vector without the need to transfect producer cells with plasmids every cycle. This increases efficiency and yield per batch. LentiStable packaging cell lines stably integrate the envelope and packaging transgenes into the cell genome so that target genes can be changed more easily.

Large-scale bioprocessing increases yield and improves purity

The TRiP system can potentially increase yield by three orders of magnitude, while improving the product quality and decreasing the cost of goods for manufacturing. It also enables the manufacturing of vectors carrying transgenes that inhibit cell growth or are cytotoxic. TRiP does not affect transgene expression in target cells. OXB is aiming to drive uptake of this technology at early research and development stages with partners and programmes that could benefit from it. This technology is patent protected to 2034 and, if utilised in commercial supply, will enable higher royalty rates on sales.

OXB's SecNuc technology streamlines the manufacturing process and reduce COGS. The industry standard for treating harvested vectors to reduce residual DNA from plasmids and host cell death in vector production uses recombinant nucleases (such as Benzonase). However, this treatment is expensive, uses elevated temperatures that can damage the vectors and commonly requires a second treatment for LVVs due to limited effectiveness. OXB's SecNuc technology optimally expresses endonucleases during vector manufacturing, negating the requirement for this purification step while also improving viral vector quality.

Validated sector-leading manufacturing capabilities

OXB is leading the industrialisation of lentivector manufacturing through significant capacity expansions and continued process innovation. Large-scale production of viral vectors is key to the

long-term commercial success of OXB's platform. OXB has more than doubled its footprint, which now extends over 226,000 sq ft with its five specialist sites.

The first phase (45,000 sq ft) of the new state-of-the-art 84,000 sq ft bioprocessing facility, Oxbox, has completed. The first two GMP suites, plus supporting areas and QC laboratories, received regulatory approval from the Medicines and Healthcare products Regulatory Agency (MHRA) in May and the first partner batches were produced in Q220. Fill and finish will also be provided in-house for the first time in this new facility, providing customers with an end-to-end offering. Instalment of the first of two fill/finish suites is expected to complete by year end. The two remaining suites have been dedicated to manufacturing the potential COVID-19 vaccine AZD1222; the first GMP suite has now received MHRA approval and has started manufacturing the vaccine. MHRA approval of the second suite is expected in October and therefore all four suites in the first phase of Oxbox are expected to be operational in Q420, significantly ahead of schedule. The remaining 39,000 sq ft is available for future expansion. OXB also expects to increase its employee headcount to over 650 by year end (584 at end H120) to fulfil the increased demand for its services.

Further manufacturing capacity is provided from OXB's additional sites. The Yarnton site (6,000 sq ft) has one GMP clean room for Process B manufacturing and the Harrow house site (4,000 sq ft) has two GMP clean rooms, providing Process A and B manufacturing capacity to meet ongoing demand for its lentiviral expertise. Multiple manufacturing facilities importantly increase the robustness of the supply chain while allowing capacity for further products and partnerships to be developed. OXB is also expanding its laboratory space and work is currently ongoing at Windrush court (32,000 sq ft) to convert office space to GMP laboratories to meet the expected near-term demand in commercial development and analytics. OXB has also invested in offices and GMP laboratories at the Windrush innovation centre (32,000 sq ft), which will focus on innovation and technological advances to support both the product pipeline and LentiVector platform.

Valuation

We value OXB at £711m vs £709m previously (Exhibit 6). We have made a number of changes to our forecasts and valuation:

- Novartis collaboration: we have added the r/r follicular lymphoma indication for Kymriah (NDA expected 2021). Assumptions for this indication are in the US and EU5 population, 0.02% prevalence of NHL, of which 20% have follicular lymphoma and 20% relapse within two years. We forecast 25% peak penetration and assume pricing of $475,000 in the US based on information from Novartis, with EU pricing at a 20% discount. We assume a peak royalty rate of 2% and an initial price to Novartis of $1.5m per vector batch. We assign 80% probability of success (NDA file 2021 and launch 2022). We have pushed back the undisclosed second CAR-T launch to 2025 from 2022 due to reduced visibility on NOVN CAR-T assets; we assume based on NOVN's R&D day presentation from December 2019 this is the BCMA-targeting CAR-T MCM998, which is being investigated in combination with a CD19 CAR-T in a Phase I study in multiple myeloma. We add in a third CAR-T programme, again undisclosed, but we assume CD22 for adult ALL in Phase I clinical trials.
- Beam Therapeutics deal: given the preclinical status and undisclosed assets we have taken one asset assumed to be a next-generation CAR-T for AML. We forecast launch in 2029. Given the minimal disclosure on this deal, we make conservative assumptions that include $2.5m in bioprocessing revenue per year between 2020–24 inclusive, manufacturing revenues and 1% royalty on sales.
- AZN: inclusion of COVID-19 revenues from the partnership (as detailed above). The £15m capacity reservation fee is guaranteed and given the circumstances of the vaccine's accelerated clinical timeline, we cautiously forecast £10m of the £35m additional revenue for

vaccine vector supply is received in 2021. We do not forecast revenues beyond the initial 18-month agreement and ascribe a 75% probability in our NPV model in line with a Phase III asset. We note that OXB could realise the full amount (£35m) as the vaccine progresses and we would need to upgrade our forecasts accordingly.

- Sanofi/Bioverativ: we have pushed back launch of the haemophilia A and B products under the partnership by a year to 2026 reflecting the planned start of clinical trials in 2022.
- Sanofi: we have removed SAR422459 for Stargardt disease and SAR421869 for Usher's syndrome.
- Orchard Therapeutics: we have delayed launch of OTL-101 for ADA-SCID by two years to 2024.
- Axovant: we have moved our forecast launch date for AXO-Lenti-PD back by two years to 2024 to better reflect the status of the ongoing Phase I/II trial.
- Following a review of its internal pipeline: work on OXB-201 (wet AMD) and OXB-202 (corneal graft rejection) have been discontinued. OXB-203 takes over from its predecessor OXB-201 for wet AMD, which we include at a 5% probability of success. We have removed OXB-202 from our valuation.

In addition, we have rolled our model forward and updated the exchange rates and net cash.

Exhibit 6: OXB valuation

	OXB products	CDMO products*	Net cash	Terminal value	Total
Total value (£m)	180.2	278.4	50.6	201.6	**710.8**
Value per share (p)	226.2	349.6	63.5	253.1	**892.5**

Source: Edison Investment Research. Note: *Excludes AXO-Lenti-PD which is included under OXB products.

A summary of the valuation by product can be seen in Exhibit 7. For detailed valuation assumptions please refer to the respective product sections throughout.

Exhibit 7: Valuation summary

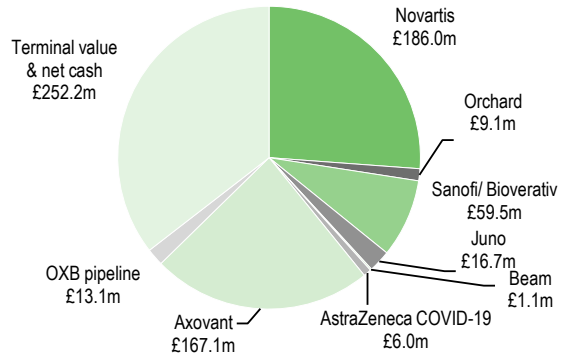
Product / partner / indication / status	Estimated launch year	Peak royalties (£m)	Peak manufacturing revenue (£m)	Probability of success	NPV (£m)	rNPV (£m)	rNPV per share (p/share)
Kymriah / Novartis / r/r pALL / Approved in US & in EU	Launched	3	2	100%	39	39	48.63
Kymriah / Novartis / DLBCL / Approved in US & in EU	Launched	23	14	100%	98	98	123.42
Kymriah / Novartis / r/r Follicular lymphoma (US NDA submission 2021)	2022	5	3	80%	28	23	28.54
2nd CAR-T / Novartis / Cancers / Phase I	2025	26	32	20%	86	22	27.44
3rd CAR-T / Novartis / Cancers / Phase I	2025	2	3	20%	22	4	5.50
OTL-101 / Orchard / ADA-SCID / Phase II/III	2024	0	1	70%	4	3	3.98
OTL-201 / Orchard / Sanf A synd / Phase I	2025	12	10	5%	36	6	7.48
Factor VIII / Bioverativ / Haemophilia A / Preclinical	2026	476	114	5%	809	44	55.69
Factor IX / Bioverativ / Haemophilia B / Preclinical	2026	119	28	5%	216	15	19.01
Juno (BMS) collaboration on undisclosed CAR-T/TCR-T therapies; assumptions are for JCAR018 in pALL and r/r NHL	2025	2	6	30%	63	17	20.98
Beam - undisclosed assumption CAR-T for AML	2029	7	1	5%	22	1	1.39
COVID-19 vaccine / AZN / AAV supply agreement	N/A	N/A	N/A	75%*	7	6	7.53
AXO-Lenti-PD / NA / Parkinson's / Phase I/II	2024	123	26	30%	469	167	209.78
OXB-302 / NA / Cancer / Preclinical	2025	61	10	5%	102	5	5.80
OXB-203 / NA / Wet AMD / Preclinical	2027	128	14	5%	165	8	10.66
Total pipeline and partnership value						**459**	**575.84**
Terminal value						**202**	**253.08**
Net cash						**51**	**63.53**
Total						**711**	**892.45**

Source: Edison Investment Research. Note: *£15m capacity reservation fee has 100% probability.

In Exhibits 8 and 9 we provide the relative partner contribution from our risk-adjusted (and unadjusted) NPVs. In all partnerships, we value the royalty, milestone and bioprocessing (manufacturing) revenues. We forecast that all non-partnered internal assets are out-licensed post Phase II data. We value all partnerships to 2040 and, due to an expanding and evolving long-term

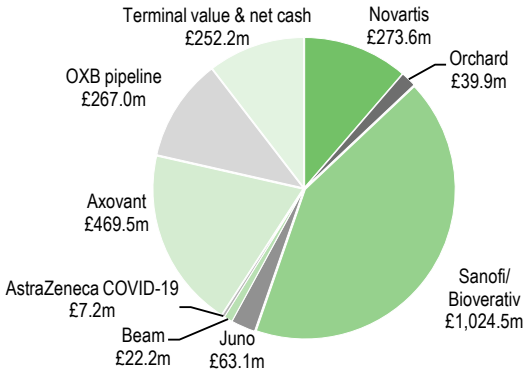
revenue stream, we include a terminal value (10% discount rate, 1% growth) for OXB, which contributes 253p/share to our valuation. We forecast that OXB will receive bioprocessing manufacturing revenue from partners throughout the collaborations and not just on commercial launch. We assume our standard 12.5% discount rate for assets, with a 10.0% discount rate for manufacturing revenues. We note that pricing of gene therapies remains a key sensitivity as the market evolves and these dynamics change, we assume pricing in the range of $350,000 to $700,000 depending on the prevalence of the disease.

Exhibit 8: Risk-adjusted NPV summary



Source: Edison Investment Research

Exhibit 9: NPV summary



Source: Edison Investment Research

OXB internal pipeline valuation assumptions

We only ascribe value to assets that have completed preclinical development and are positioned for out-licensing and/or further clinical development. We thus value OXB-203 (wet AMD, preclinical), and OXB-302 (cancer, preclinical) and assume all will be out-licensed following Phase I/II data. We also include AXO-Lenti-PD (OXB-102) in PD, which was originally developed by OXB before out-licensing to Axovant. We forecast that all are priced at $350,000 in the US, with a 20% discount in EU. We assume partners will use OXB's manufacturing capabilities to provide vectors at $1.5m per batch, with peak gross margins of 30%.

Exhibit 10: OXB's internal proprietary pipeline

Product	Indication (area)	Stage of development	Probability of success	Notes
AXO-Lenti-PD (OXB-102)	Parkinson's disease	Phase I/II (SUNRISE-PD)	30%	We assume an incidence of 0.028% for PD, of which 65% can be treatment and peak penetration of 5%. We model a 7–8% royalty rate and forecast launch in 2024.
OXB-302	Multiple haematological and solid tumours (oncology)	Preclinical	5%	No specific cancer has been chosen for development so we have assumed it is used in DLBCL with an incidence of non-Hodgkin's lymphoma of 0.02%, of which 48% of patients have DLBCL, 35% fail first- and second-line treatments and a peak penetration of 10%. We assume a 15% royalty rate and forecast launch in 2025.
OXB-203	Wet AMD (ophthalmology)	Preclinical	5%	We assume 2% of the population have AMD, of which 10% have wet AMD, 10% of patients can be treated, and a peak penetration of 2.5%. We assume a 15% royalty rate and forecast launch in 2027.

Source: Oxford Biomedica, Edison Investment Research

Financials

OXB reported H120 revenues of £34m (+6% y-o-y from £32.1m). Licence fees, milestones and royalty (LMR) revenue declined to £10.6m in H120 vs £13.3m in H119, as H119 benefited from $15m (£11.5.m) development milestone received from Axovant related to progress of AXO-Lenti-PD. LMR revenue in H120 comprised an $8m (£6.2m) upfront licence payment received from Juno/BMS and, although undisclosed, we assume most of the remainder is £4.4m in royalties for Kymriah. License and milestones payments are lumpy and volatile in nature and will vary year on year given OXB's propensity to sign new deals and expand on existing ones.

Bioprocessing/commercial development revenues, which are historically more predictable, grew to £23.4m (+24% y-o-y from £18.8m), driven by a greater volume of development activity, notably for Juno/BMS, Beam and the Cystic Fibrosis Consortium. Revenues from the production of clinical and commercial batches increased due to higher numbers of batches bioprocessed for Orchard, Juno/BMS and Axovant.

R&D and bioprocessing costs increased to £15.2m (H119: £12.5m) and £9.2m (H119: £4.1m) in H120. The increase in bioprocessing costs is a result of headcount, facility costs and related spend on Oxbox. We include forecast bioprocessing costs in our R&D line, previously included in cost of sales. Our FY20 COGS forecast is £25.9m and R&D and bioprocessing costs have increased to £51.8m, reflecting the reportioning of costs. Administrative costs rose to £4.7m (vs £4.0m in H119) and we retain our full-year forecast of £12.2m as we expect an uptick in H220 given the expected increase in the number of employees by year end.

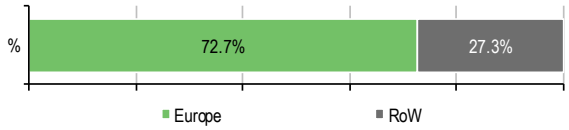
Capital expenditure in H120 was £5.3 (vs £14.3m in H119), as the comparator period was driven mainly by the build and fit of Oxbox and the expansion of the business as a whole. Capex is expected to rise in H220, reflecting cost of converting office space in Windrush Court to GMP laboratories and completion of the first fill and finish line at Oxbox. We maintain our forecast FY20 capex of £15.0m.

Net cash was £50.6m at 30 June (vs £16.2m at 31 December 2019), reflecting the £40m capital (£38.6m net of expenses) raise in the period (June). We have adjusted our FY20 revenue forecasts of £84.2m (from £76.5m previously), reflecting the £10m from AZN as guided by management, and now forecast an operating loss of £5.8m in FY20, but note that multiple sensitivities remain around this figure, including cost sensitivities in R&D, facilities and personnel, in addition to revenue sensitivities with regard to Kymriah sales growth, the extent of bioprocessing revenue, milestone payments and the execution of any new deals. We cautiously forecast £10m of the £35m additional revenue for vaccine vector supply is received in FY21. We do not forecast revenues beyond the initial 18-month agreement and note that OXB could realise the full amount (£35m) as the vaccine progresses and we would need to upgrade our forecasts accordingly.

Exhibit 11: Financial summary

Accounts: IFRS; year-end 31 December; £000s	2016	2017	2018	2019	2020e	2021e
INCOME STATEMENT						
Total revenues	27,776	37,590	66,778	64,060	84,229	112,379
Cost of sales	(11,835)	(18,442)	(33,261)	(35,723)	(25,943)	(42,097)
Gross profit	15,941	19,148	33,517	28,337	58,286	70,282
Administrative expenses	(5,957)	(7,276)	(7,433)	(11,881)	(12,237)	(14,685)
R&D and bioprocessing costs	(24,299)	(21,611)	(19,216)	(29,924)	(51,822)	(44,102)
Other income/(expense)	3,002	1,774	1,064	884	0	0
Exceptionals and adjustments	0	2,297	5,983	(1,883)	0	0
Operating profit/(loss)	(11,313)	(5,668)	13,915	(14,467)	(5,773)	11,495
Finance income/(expense)	(8,994)	(6,093)	(8,901)	(6,422)	207	252
Reported PBT	(20,307)	(11,761)	5,014	(20,889)	(5,566)	11,747
Income tax expense (includes exceptionals)	3,666	2,744	2,527	4,823	5,064	(2,232)
Reported net income	(16,641)	(9,017)	7,541	(16,066)	(502)	9,515
Basic average number of shares, m	55.6	61.9	65.2	72.7	79.6	82.1
Basic EPS (p)	(29.9)	(14.6)	11.6	(22.1)	(0.6)	11.6
Adjusted EBITDA	(6,773)	(2,645)	13,535	(4,550)	2,176	19,860
Adjusted EBIT	(10,448)	(7,020)	9,178	(10,337)	(5,773)	11,495
Adjusted PBT	(19,442)	(13,113)	277	(16,759)	(5,566)	11,747
Adjusted EPS (p)	(28.4)	(16.7)	4.3	(16.4)	(0.6)	11.6
BALANCE SHEET						
Property, plant and equipment	27,514	25,370	31,791	61,932	68,951	72,566
Intangible assets	1,330	97	117	95	95	95
Other non-current assets	657	2,954	10,966	0	0	0
Total non-current assets	29,501	28,421	46,874	65,991	73,272	76,886
Cash and equivalents	15,335	14,329	32,244	16,243	41,389	50,485
Inventories	2,202	3,332	4,251	2,579	4,620	4,613
Trade and other receivables	6,904	17,088	26,585	30,045	28,846	38,486
Other current assets	3,000	2,232	2,446	8,070	7,783	2,719
Total current assets	27,441	36,981	65,526	56,937	82,638	96,303
Non-current loans and borrowings	34,389	36,864	41,153	0	0	0
Contract liabilities and deferred income	0	0	6,434	5,005	5,005	5,005
Other non-current liabilities	622	630	1,566	13,352	13,614	15,846
Total non-current liabilities	35,011	37,494	49,153	18,357	18,619	20,851
Trade and other payables	6,003	8,690	11,422	14,297	8,885	14,417
Contract liabilities and deferred income	3,313	13,072	17,084	14,162	14,162	14,162
Total current liabilities	9,316	21,762	28,506	28,941	23,529	29,061
Equity attributable to company	12,615	6,146	34,741	75,630	113,762	123,277
CASH FLOW STATEMENT						
Operating profit/(loss)	(11,313)	(5,668)	13,915	(14,467)	(5,773)	11,495
Depreciation and amortisation	3,675	4,375	4,357	5,787	7,950	8,365
Share based payments	865	945	1,246	2,247	0	0
Other adjustments	(579)	(1,326)	(8,012)	1,886	0	0
Movements in working capital	1,423	141	(2,292)	(2,089)	(6,254)	(4,102)
Income taxes paid	4,081	4,512	3,654	3,128	5,351	5,064
Cash from operations (CFO)	(1,848)	2,979	12,868	(3,508)	1,274	20,823
Capex	(6,458)	(1,969)	(10,148)	(25,774)	(14,969)	(11,979)
Other investing activities	47	38	52	104	207	252
Cash used in investing activities (CFIA)	(6,411)	(1,931)	(10,096)	(19,398)	(14,762)	(11,727)
Net proceeds from issue of shares	17,497	385	19,808	53,363	38,634	0
Movements in debt	0	8,361	0	(43,589)	0	0
Interest paid	(3,258)	(10,800)	(4,665)	(2,513)	0	0
Other financing activities	0	0	0	0	0	0
Cash from financing activities (CFF)	14,239	(2,054)	15,143	6,905	38,634	0
Increase/(decrease) in cash and equivalents	5,980	(1,006)	17,915	(16,001)	25,146	9,096
Currency translation differences and other	0	0	0	0	0	0
Cash and equivalents at beginning of period	9,355	15,335	14,329	32,244	16,243	41,389
Cash and equivalents at end of period	15,335	14,329	32,244	16,243	41,389	50,485
Net (debt)/cash	(19,054)	(22,535)	(8,909)	16,243	41,389	50,485

Source: Oxford Biomedica accounts, Edison Investment Research

Contact details	Revenue by geography
Windrush Court Transport Way Oxford OX4 6LT United Kingdom +44 (0) 1865 783 000 www.oxfordbiomedica.co.uk	

Management team

CEO: John Dawson	CFO: Stuart Paynter
John joined as non-executive director in August 2008 and was appointed CEO in October 2008 (he was acting CEO from August to October 2008). He previously worked at Cephalon (2008–14), including as CFO and head of BD Europe.	Stuart joined as CFO in August 2017. He previously held multiple roles at Shire Pharmaceuticals including senior director of finance business partnering and global head of internal audit. Prior to joining OXB, he was head of finance business partnering at De La Rue.

Principal shareholders	(%)
Vulpes Investment Management	13.0
M&G Investment Management	11.4
Novo Holdings	10.0
Lionstrust Asset Management	4.0
Hargreaves Lansdown Asset Management	3.9
Mr S Shah	3.6
Artisan Partners	3.4
Aviva	3.1
Nine Ten Capital Management	3.0

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